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TI Mammalian auditory hair cell regeneration/repair and protection: a review and future directions.
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AB Regeneration/repair and protection of auditory hair cells and auditory neurons is an exciting, rapidly evolving field. Simultaneous developments in the fields of otobiology and surgical otology have led to new and exciting possibilities in inner ear medicine and surgery; specifically, the treatment or prevention of a variety of types of **hearing losses** in the foreseeable future. **Sensorineural hearing loss** in humans is commonly associated with a loss of auditory hair cells. It has been generally accepted that **hearing loss** resulting from hair cell damage is irreversible because the human ear has been considered to be incapable of regenerating or repairing these sensory elements following severe injury. An organ of Corti explant study has shown that it is possible to initiate the regeneration/repair of mammalian hair cells. In this study, ototoxin-damaged organ of Corti explants from juvenile rats were treated with a combination of retinoic acid (10-8M) and fetal calf serum (10%). TGF-alpha has been identified as a growth factor capable of evoking auditory hair cell regeneration/repair in ototoxin-damaged organ of Corti explants. Preliminary in vitro experiments with juvenile rat organ of Corti explants and in vivo studies in the cochleae of adult guinea pigs indicate that pretreatment followed by continuous treatment of the inner ear with a combination of retinoic acid and TGF-alpha can protect the auditory hair cells from the ototoxic effects of aminoglycosides. Because the integrity of spiral ganglion neurons is also essential for normal auditory function, there is a parallel series of in vitro and in vivo studies of the effects of **neurotrophic** factors on the survival of auditory neurons and the regeneration of injured neuronal processes. Clinical studies have demonstrated that it is now possible to perform surgeries on the inner ear, i.e., partial or total labyrinthectomies, and maintain hearing. The field of cochlear implantation has also provided insights into both the short- and long-term effects of cochlear fenestration on inner ear function. Administration of growth factors to the inner ears of animals is now possible with the use of implanted catheters and miniature infusion pumps. These advances suggest that localized application of drugs to the human inner ear may be feasible. The aim of this paper has been to provide an overview of advances in the study

of the biology of auditory hair cells and auditory neurons, as well as recent relevant surgical advances. Taken together, these advances in otobiology and surgery will, in the future, be combined to devise new and innovative treatments for inner ear disorders.

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